American Journal of Epidemiology
Vol. 153, No. 9
Printed in U.S.A.

ORIGINAL CONTRIBUTIONS

Leukemia, Brain Tumors, and Exposure to Extremely Low Frequency Electromagnetic Fields in Swiss Railway Employees

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Railway engineers provide excellent opportunities for studying the relation between exposure to extremely low frequency magnetic fields and leukemia or brain tumors. In a cohort study of Swiss railway personnel with 2.7×10^5 person-years of follow-up (1972–1993), the authors compared occupations with high average exposures (line engineers: 25.9 μT) to those with medium and low exposures (station masters: 1 μT). The mortality rate ratio for leukemia was 2.4 (95% confidence interval (CI): 1.0, 6.1) among line engineers (reference category: station masters). The mortality rate ratio for brain tumors was 1.0 (95% CI: 0.2, 4.6) among line engineers and 5.1 (95% CI: 1.2, 21.2) among shunting yard engineers (compared with station masters). Two exposure characteristics were evaluated: cumulative exposure in μT-years and years spent under exposure to magnetic fields of ≥10 μT. There was a significant increase in leukemia mortality of 0.9% (95% CI: 0.2, 1.7) per μT-year of cumulative exposure to extremely low frequency magnetic fields. The increase by years spent under exposure of ≥10 μT was even stronger: 62% per year (95% CI: 15, 129). Brain cancer risk did not show a dose-response relation. This study contributes to the evidence for a link between heavy exposure to extremely low frequency magnetic fields and leukemia. Its strengths include reliable measurements and reliable historical reconstruction of exposures. *Am J Epidemiol* 2001;153:825–35.

brain neoplasms; electromagnetic fields; environmental monitoring; leukemia; occupational exposure

Editor's note: *An invited commentary on this article appears on page 836, and the authors' response appears on page 839.*

Several papers (1–3) reviewing residential and occupational epidemiologic studies of cancer risks and exposure to extremely low frequency (ELF) magnetic fields have concluded that there is a weak association between exposure to electromagnetic fields and leukemia and brain tumors. Several occupational epidemiologic studies have explored the relation between ELF magnetic field exposure and leukemia or brain tumors (4–10), with contradictory findings. Kheifets et al. (2) have investigated the causes of discrepancies in studies of brain cancer and have suggested many possible reasons for these discrepancies. However, it is evident that one of the principal challenges of studies of the health effects of ELF magnetic fields is exposure assessment, since historical measurements are usually lacking (11, 12). High-quality work in this area has been conducted by Feychting and Ahlbom (13) for residential exposure and by Savitz and Loomis (8) for occupational exposures.

In Switzerland, the study of railway workers offers an excellent possibility for investigating the health effects of ELF magnetic fields. Exposures of railway engineers can be measured and extrapolated accurately, since the position of a train's driver is fixed and electromagnetic characteristics stay the same over the lifetime of an engine, thus permitting reliable extrapolation. In addition, the Swiss railways have extensive, mostly electronic records on their employees, which allows cohort studies. An earlier study showed excess mortality from malignancies of the hematopoietic and lymphatic systems for engineers as compared with workers in metal construction and engineering and technical personnel (14). Subsequently, measurements of ELF magnetic fields in Swiss railway engines were made, showing magnetic field strengths in the 3–6,000 μT range at the workplaces of railway engineers (15).

The purpose of the present study was to use better methodology to reassess whether, for Swiss railway engineers, exposure to electromagnetic fields is associated with an increased risk for leukemia or brain tumors. In particular, we wanted to investigate the following two hypotheses (adapted from the original project funding proposal from 1991, with slightly changed wording):

1. *Occupational hypothesis.* Among four groups of railway employees—line engineers, shunting yard engi-

Received for publication March 15, 2000, and accepted for publication August 10, 2000.

Abbreviations: CI, confidence interval; ELF, extremely low frequency; ICD-8, *International Classification of Diseases*, Eighth Revision.

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neers, train attendants, and station masters (defined more precisely below)—the groups with higher exposures to ELF magnetic fields experience higher mortality from leukemia and brain tumors than those with lower exposures.
2. *Dose-response hypothesis.* Independent of job description, there is a dose-response relation between leukemia and brain cancer mortality and cumulative exposure to ELF magnetic fields and time spent exposed to ELF magnetic fields of ≥10 μT.

MATERIALS AND METHODS

Cohort

The cohort was established using Swiss Federal Railways personnel and pension records. The cohort comprised all male persons recorded as actively employed or retired and alive in the microfiche copies of personnel or pension records from 1972, 1974, and 1978 or in the computer tapes of the Federal Railways Personnel and Pension Department between 1980 and 1993. Only members of four job categories—line engineer, shunting yard engineer, train attendant, and station master—were considered.

Vital status and cause of death

Mortality follow-up covered the period between January 1, 1972, and December 31, 1993. Probabilistic record linkage (16, 17) was used to determine the vital status and mortality endpoints of cohort members by linking personnel or pension records to (anonymous) death certificates. Linkage variables used were date of birth, date of death, place of residence, occupation, marital status, and duration of marriage if married. Prior to linking, knowledge of the vital status of cohort members was completed by searching union journals and noting all deaths in the four study job categories. The computerized records of death certificates were then matched by name and date of birth to personnel or pension records. Only deaths with complete agreement regarding dates of birth and death on the personnel or pension record and the death certificate and with an odds ratio for correct linkage (vs. linkage due to random agreement) exceeding 1,024 were accepted. Finally, the vital status of all 123 linked cases with a cause of death of leukemia, other hematopoietic or lymphatic neoplasm, or brain tumor were manually verified against archived pension records. The data sources (personnel records, pension records, and death certificates) and linkage variables used did not differ between occupations.

Outcomes

The main mortality outcomes were leukemia (*International Classification of Diseases*, Eighth Revision (ICD-8), codes 204–207; 37 cases) and brain tumors (ICD-8 code 191; 23 cases) (18). In addition, we analyzed deaths from any cause, all cancer deaths, and lung cancer deaths (ICD-8 code 162) for validation purposes. Table 1 gives the numbers of deaths in each category, including leukemia subtypes.

Work situation

Swiss railway employees work 8-hour days, 5 days per week. Line engineers and train attendants are on rotating shift work, beginning with the late shift at 4:00 p.m. and moving forward 1 hour each day until they are on the early shift, beginning around 4:00 a.m. After each cycle of shift work, they are off work for 3–4 days. Line engineers are the drivers of all scheduled trains. Mostly, they drive large and powerful engines. Each line engineer drives several different engines daily, with a changing composition of engines over time. Shunting yard engineers drive smaller engines around the shunting yards, setting up train compositions. They also switch between engines. Train attendants accompany passenger trains, checking tickets and assisting travelers. Station masters are responsible for train traffic within a station perimeter. They work partly in an office and partly on the station platforms.

Employment data with beginning and ending dates, duration, and job category were available for all cohort members. We assigned each person to the job category last mentioned. With few exceptions, this corresponded to the job held the longest, since there was limited switching between job categories. However, younger line engineers often worked in shunting yards (M. Gerber, Motive Power Construction Division, personal communication, 2001).

Assessment of magnetic field exposure

Swiss trains run on 16⅔-Hz alternating current. For our measurements, we used a device developed by Bramur, Inc. (Lee, Massachusetts). Tests conducted at the technical laboratory of Swisscom (Berne, Switzerland) confirmed that it was reliable for recording magnetic flux density in the frequency range between 0 Hz and 100 Hz. Measurements of root mean square field strength were taken at 10-second intervals and stored in a battery-powered computer. Figure 1 shows the readings from one driving cycle. The raw readings were processed to extract mean exposure, as well as the time fraction with field strength at or above 10 μT. This fraction is a simple measure of exposure dynamics.

Exposure assessment for line and shunting yard engineers. For measurements of exposure in the driver's seat of the engine, three measuring heads were mounted on a wooden stand just behind the driver at the level of his head, thorax, and feet without the use of metal parts. For each major type of engine that had been used in Switzerland since 1905, measurement series covering complete driving cycles (starting, acceleration phase, driving phase, braking, and stopping) lasting from 20 minutes to 4 hours were taken. For the most numerous engines, the impact of the kind of train (freight train, normal train, or fast train) and the particular route taken on the magnitude of the magnetic fields was examined. The variability within a specific type of engine was found to be moderate (coefficients of variation of mean exposure per time unit calculated from one driving cycle did not exceed 26 percent).

TABLE 1. Numbers of workers exposed to extremely low frequency electromagnetic fields and numbers of deaths, by cause and occupation, Swiss railway cohort, 1972–1993

	Occupation				
	Line engineer	Shunting yard engineer	Train attendant	Station master	Total cohort
No. exposed	6,879	1,314	5,720	4,157	18,070
No. of deaths, by cause					
All causes (000–999)*	1,152	244	1,315	868	3,579
All cancers (140–209 and 225)	388	88	391	256	1,123
Lung cancer (162)	77	20	88	58	243
Malignancies of the hematopoietic and lymphatic systems (200–209)	40	11	26	21	98
Leukemias (204–207)	19	3	9	6	37
Chronic lymphatic leukemia (204.1)	7	1	2	6	16
Chronic myeloic leukemia (205.1)	6	0	2	0	8
Acute lymphatic leukemia (204.0)	0	0	1	0	1
Acute myeloic leukemia (205.0)	3	2	3	0	8
Other (204.9, 205.9, 206, and 207)†	3	0	1	0	4
Brain tumors (191)	4	5	11	3	23

* Numbers in parentheses, *International Classification of Diseases*, Eighth Revision (18), code(s).
† Monocytic leukemia and further nonspecifically coded diagnoses in the death registry.

For modified engines in which exposure was not measured, the measurements of the corresponding main type of engine were used.

Calculation of historical exposure. Swiss line engineers switch engines several times daily, and over time they drive a changing mix of engines. We obtained the numbers of engines

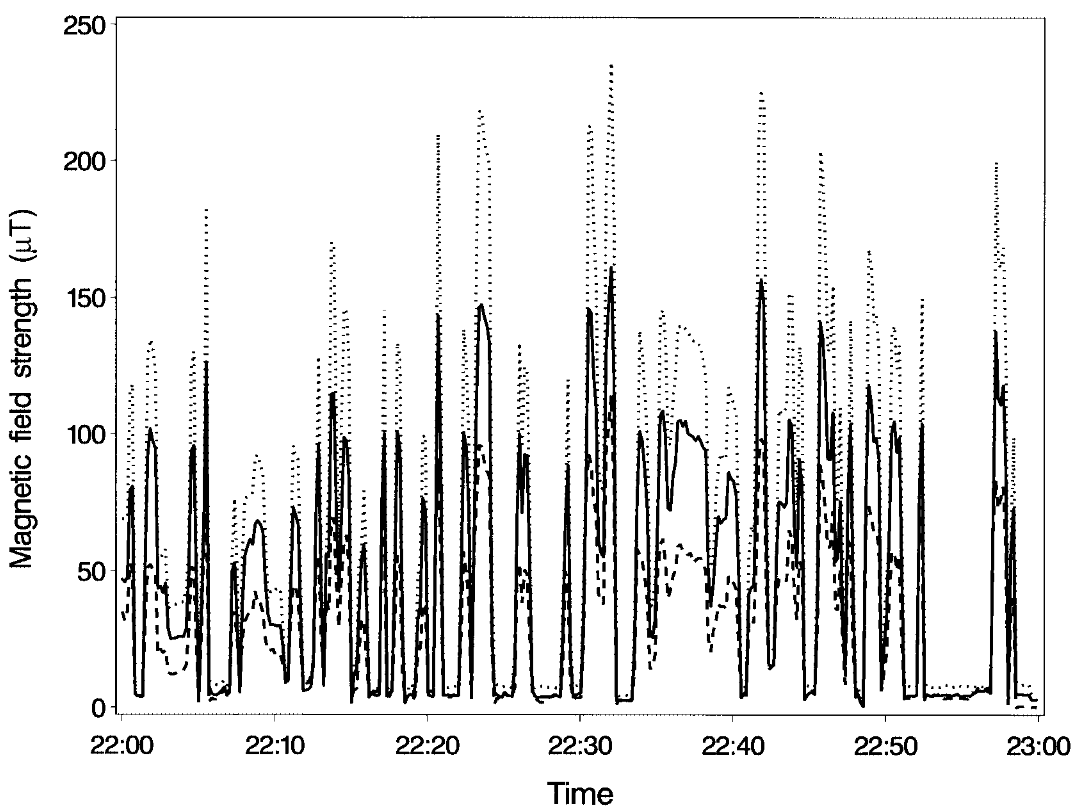

FIGURE 1. Graphic representation of exposure levels measured at 10-second intervals during one driving cycle in a line engine, Swiss railway cohort, 1972–1993. Solid line: head; dotted line: thorax; dashed line: feet.

in service every 5 years from 1905 to 1995 and estimated the ELF magnetic field load for each 5-year calendar period by calculating weighted averages of engine-specific exposures. A similar approach was used to estimate the historical exposure of shunting yard engineers, including an average of 36 percent steam-powered engines (1905–1965) and later diesel-electric engines (1954–1995). We assumed that steam-powered and diesel-electric engines gave zero exposures (diesel-electric engines being direct-current engines).

For independent validation of the historical exposure reconstruction, we assembled the engine sequences of the daily service tours of 52 line and 14 shunting yard engineers for several weeks in 1993 (19).

Exposure assessment for train attendants and station masters. Train attendants and station masters do not work at the same location for extended periods of time. Therefore, spot measurements lasting for 2–30 minutes were taken at their most frequent places of work (train attendants: various positions within the coaches; station masters: platform and office). Exposure was then estimated as a time-weighted average of location-specific field strengths. The weights were estimated in close collaboration with railway authorities, taking into account the fractions of air-conditioned and electrically powered coaches.

Calculation of historical exposure. For train attendants and station masters, only recent measurements were available. Historical exposures were linearly interpolated between 0 μT for 1900 and the exposure level of 1993.

Data analysis

Data were analyzed using SAS (20) and Stata (21). Record linkage was carried out using probabilistic linkage with the LinkPro subroutine package (17). For cohort analysis, we used Clayton's algorithm as described by Breslow and Day (22), with 5-year age groups/5-year periods/exposure categories as units of analysis. The cumulative exposures were classified into three categories: 0–4.99 μT-years, 5.00–74.99 μT-years, and ≥75 μT-years. We determined these cutoffs from the empirical frequency distribution of cumulative exposure to obtain an approximately equal distribution of person-years across the exposure categories. Similarly, the time fractions of each year spent under ELF magnetic field exposures of ≥10 μT were cumulated over life. These were aggregated into the following groups: ≤0.099 years, 0.100–0.499 years, and ≥0.50 years (feet: ≤0.199 years, 0.2–0.499 years, and ≥0.5 years).

To estimate mortality rate ratios and their 95 percent confidence intervals, we carried out Poisson regressions using number of deaths from leukemia or brain cancer per unit of analysis (see above) as the dependent variable and 5-year age group, 10-year calendar period, and job or exposure category as the independent variables. For estimation of the dose-response curves, we classified exposures into five classes by subdividing the lowest class and the middle class. The number of person-years at risk was included as an offset in the models. We carried out trend analyses using weighted regression with mortality rate ratios as dependent variables and job-related exposures as independent variables.

RESULTS

Basic information on the cohort is presented in tables 1 and 2. There were 18,070 cohort members and 270,155 person-years of mortality follow-up.

Information on linkage

Manual mortality follow-up in union periodicals yielded 1,729 records—8.2 percent of all engineers and 10.7 percent of all train attendants and station masters. Restricting linkage to those links in which dates of birth and death agreed resulted in the loss of 147 (4.1 percent) potentially linkable deaths. Manual checking of 121 linked cancer deaths resulted in our finding one person who was still alive; i.e., one incorrect link was discovered.

Each cohort member was assigned the job he held when he left the cohort. Job changes were not frequent. Fifteen percent of shunting yard engineers were promoted to the position of line engineer. Fewer than 2 percent of line engineers changed to shunting yard engineer, and none became train attendants or station masters. Fewer than 2 percent of station masters and train attendants changed their job category.

Accuracy of exposure information

Treating the engine mix driven by each line engineer as a random sample of all engines available at the time, the coef-

TABLE 2. Demographic and employment information for workers exposed to extremely low frequency electromagnetic fields, by occupation, Swiss railway cohort, 1972–1993

Occupation	Person-years of observation (1972–1993)	Median duration of employment (years)	Median year of starting work	% actively employed on January 1, 1972*	Median age (years) on January 1, 1972*
Line engineer	94,168	24.6	1968	90.1	47
Shunting yard engineer	22,116	32.4	1958	94.5	43
Train attendant	88,986	34.0	1956	86.6	48
Station master	64,886	39.5	1952	87.9	41
Total	270,155 †	33.0	1958	88.8	46

* Excludes those who entered the cohort after January 1, 1972.
† Differs from sum because of rounding imprecision.

ficient of variation of the cumulative occupational exposure reconstruction was estimated at 18 percent for the head, 25 percent for the thorax, and 40 percent for the feet. For shunting yard engineers, the coefficient of variation of the reconstructed estimate of cumulative exposure was estimated to be 26 percent regardless of body location. Estimates of cumulative exposure obtained by reconstructing average exposure using the daily work plans of 52 line engineers and 14 shunting yard engineers over a 2-week period were within 10 percent of the historical reconstruction estimates described above. For station masters, the coefficient of variation of the reconstruction was approximately 40 percent. For train attendants, the coefficient varied from 25 percent at the head and thorax levels to 60 percent at the feet.

Table 3 shows the exposure characteristics of the four occupations for the years 1930, 1960, and 1990. There was a fairly steady increase in the estimated exposure levels.

To assess the quality of endpoints, we checked mortality outcomes against cancer registry data. Not all of Switzerland is covered by cancer registries. For deceased cohort members with a diagnosis of malignancy on their death certificates who had lived in an area covered by a cancer registry, we verified the diagnosis against the corresponding cancer registry entry. This applied to 11 out of 37 cases of leukemia and 12 out of 23 cases of brain tumor. For two of 12 brain tumors on death certificates, the three-digit ICD-8 diagnosis was misspecified. Of the 11 leukemias on death certificates, all were classified as leukemias in the cancer registry files.

TABLE 3. Characteristics of low frequency electromagnetic fields, Swiss railway cohort, 1972–1993

Occupation and year of exposure	Mean exposure (μT-years)	% of time exposed to fields ≥10 μT*
Line engineer		
1930	9.3	9.9
1960	17.9	29.5
1990	25.9	47.5
Shunting yard engineer		
1930	2.6	1.4
1960	13.4	9.7
1990	13.4	9.7
Train attendant		
1930	0.4	0.4
1960	1.9	2.2
1990	3.3	3.6
Station master (reference group)		
1930	0.1	0.0
1960	0.6	0.0
1990	1.0	0.0

* Percentage of working time spent under exposures of ≥10 μT.

Study hypotheses

To assess the occupational hypothesis (see Introduction), we calculated mortality rate ratios for five causes of death and three job categories—line engineers, shunting yard engineers, and train attendants—each compared with station masters (table 4). No differences between occupations were apparent for all-cause mortality or lung cancer mortality. However, there appeared to be differences in leukemia mortality between engineers on the one hand and train attendants and station masters on the other, although statistical significance was not attained. Risk of brain tumor mortality appeared to be elevated for shunting yard engineers and train attendants, but only the shunting yard engineers' risk relative to that of station masters was significant.

The association between occupational leukemia mortality rate ratios from table 4 and mean exposures from table 3 for these occupations in 1930 proved to be significant (p for trend = 0.04), as did the associations for the years 1960 ($p = 0.03$) and 1990 ($p = 0.03$). The associations between occupational leukemia risks and the fractions of time members of these occupations spent under magnetic fields ≥10 μT in strength were also significant (p's for trend < 0.05 for 1930, 1960, and 1990). None of the analogous associations of exposure and brain tumor mortality risk were significant. Thus, the occupational hypothesis was confirmed for leukemia and refuted for brain tumors.

To assess the dose-response hypothesis (see Introduction), we estimated a dose-response curve by including all occupations together in a Poisson regression with number of leukemia (or brain tumor) deaths as the dependent variable, offset person-years at risk (22, p. 137), and the independent variables age group, calendar period, and exposure category. The results are shown in table 5 for various measures of exposure. For leukemia, there was an excess risk in the highest exposure category regardless of the way exposure was assessed. This excess attained significance for time spent under ELF magnetic fields ≥10 μT at the thorax level; it did not reach significance at the other body sites or for mean exposure. For brain tumors, no consistent increase in risk with dose was visible, regardless of the measure used. However, the lowest category seemed to have a lower risk—significantly so for time spent under ELF magnetic fields ≥10 μT at the level of the feet.

On the basis of the fairly steady increase in leukemia mortality risk by exposure seen in table 5, we carried out Poisson regression analyses using exposure as a continuous linear covariable, thus obtaining a more powerful analysis. These results are presented in table 6. With every measure of exposure, a significant increase in the mortality rate ratio with exposure was obtained; the largest and most significant effect estimates were for years under ELF magnetic fields ≥10 μT at the head and thorax levels. The analyses of table 6 confirm the dose-response hypothesis for leukemia. We conducted a sensitivity analysis incorporating both job classification and exposure for the leukemia deaths. While both the effects of job classification and the effect of exposure became insignificant, the estimate of percentage increase in leukemia mortality per μT-year of cumulative thorax exposure increased from 0.94 percent to 1.46 percent (95 percent CI: −1.15, 4.1).

TABLE 4. Risk ratios (adjusted for age and calendar period) for various causes of death among workers exposed to extremely low frequency electromagnetic fields, by occupation, Swiss railway cohort, 1972–1993

Cause of death	Occupation (reference group: station masters)					
	Line engineer		Shunting yard engineer		Train attendant	
	RR*	95% CI*	RR	95% CI	RR	95% CI
All causes	1.01	0.93, 1.11	1.08	0.94, 1.25	1.07	0.98, 1.17
All neoplasms (140–209 and 225)†	1.14	0.97, 1.34	1.21	0.95, 1.54	1.07	0.91, 1.25
Leukemias (204–207)	2.44	0.97, 6.11	2.00	0.50, 8.07	1.09	0.39, 3.05
Brain tumors (191)	1.02	0.23, 4.55	5.06	1.21, 21.2	2.67	0.75, 9.62
Lung cancer (162)	0.98	0.70, 1.38	1.12	0.67, 1.86	1.04	0.75, 1.45

* RR, risk ratio; CI, confidence interval.
† Numbers in parentheses, *International Classification of Diseases*, Eighth Revision (18), code(s).

Confounder assessment

Engineers were not involved in the cleaning and maintenance of railway engines. Cleaners in use during the study period were phosphatic and sulfuric acids and, later, formic acid. Benzene was never used as a cleaning fluid (P. Lauber, Cleaning Services, personal communication, 2001). Polychlorinated biphenyls were never used in Swiss Railways transformers (M. Gerber, Motive Power Construction Division, personal communication, 2001). Line and shunting yard engineers receive periodic medical checkups, including chest radiographs. These could lead to, at most, 0.3 cases of leukemia over the whole lifetime of our cohort (estimate of the Swiss Workers' Accident Insurance Fund, December 13, 1989). In an unpublished survey of 378 railway employees carried out in 1994, we found that station masters and line engineers had the smallest fractions of smokers (8 percent and 12 percent, respectively), while shunting yard engineers and train attendants smoked more frequently (38 percent and 29 percent, respectively).

TABLE 5. Risk ratios (adjusted for age and calendar period) for leukemia and brain cancer mortality among workers exposed to extremely low frequency electromagnetic fields, by location and measure of exposure, Swiss railway cohort, 1972–1993

Measure of exposure and site of measurement	Person-years of follow-up*	Leukemia (ICD-8† codes 204–207)				Brain tumors (ICD-8 code 191)			
		No. of deaths	Crude RR†	Adjusted RR	95% CI†	No. of deaths	Crude RR	Adjusted RR	95% CI
Cumulative exposure (μT-years)									
Thorax									
0–4.9‡	32,753	6	1.00	1.00		1	1.00	1.00	
5–74.9	108,500	9	0.45	0.78	0.27, 2.24	11	3.32	2.84	0.35, 22.9
≥75	128,902	22	0.93	1.64	0.64, 4.19	11	2.80	2.36	0.29, 19.3
Years spent under extremely low frequency electromagnetic fields of ≥10 μT									
Head									
0.0–0.099‡	32,777	6	1.00	1.00		1	1.00	1.00	
0.1–0.49	107,811	9	0.46	0.78	0.27, 2.24	11	3.24	2.83	0.35, 22.8
≥0.5	129,568	22	0.93	1.65	0.65, 4.20	11	2.78	2.38	0.29, 19.4
Thorax									
0.0–0.099‡	88,427	9	1.00	1.00		4	1.00	1.00	
0.1–0.49	86,265	6	0.68	0.97	0.33, 2.81	12	3.08	2.55	0.80, 8.14
≥0.5	95,463	22	2.27	2.43	1.10, 5.36	7	1.62	1.27	0.37, 4.42
Feet									
0.0–0.199‡	75,856	6	1.00	1.00		3	1.00	1.00	
0.2–0.49	99,774	12	1.52	1.54	0.57, 4.12	11	2.79	3.89	1.06, 14.2
≥0.5	94,525	19	2.54	2.08	0.82, 5.29	9	2.41	1.45	0.39, 5.40

* Differences in totals are due to rounding imprecision.
† ICD-8, *international Classification of Diseases*, Eighth Revision (18); RR, risk ratio; CI, confidence interval.
‡ Reference group.

TABLE 6. Estimated increase in leukemia mortality due to exposure to extremely low frequency electromagnetic fields, based on different measures of exposure, Swiss railway cohort, 1972–1993

Exposure measure	% increase per year of exposure*	95% confidence interval
Cumulative exposure at thorax (μT-years)	0.94	0.225, 1.65
Years spent under extremely low frequency electromagnetic fields of ≥10 μT		
Head	62	15, 129
Thorax	78	22, 161
Feet	53	7, 118

* This quantity corresponds to 100 × (mortality rate ratio − 1), with the mortality rate ratio corrected for age (linear and quadratic), period, and exposure.

DISCUSSION

Findings

The results of the present study demonstrated a dose-response relation between leukemia mortality and occupational exposure to 16⅔-Hz magnetic fields. The picture of this excess mortality was consistent: It occurred in the highly exposed occupational groups, as well as in persons with high exposures. Even within each occupation, more highly exposed persons were at higher risk, although this relation was no longer significant. A dose-response relation was observable using different measures of exposure: cumulative exposure at the thorax level as well as cumulative time spent under exposures ≥10 μT at the head, thorax, and feet. There was a statistically stronger and more significant association of leukemia risk with length of exposure to ELF magnetic fields at levels of ≥10 μT than with cumulative exposure at the thorax level. This could indicate that the dynamics of the exposure process play a more important role than has been suspected so far. An important health effect of exposure dynamics would provide an explanation for the inconsistent results found in occupational and residential studies of the health effects of ELF magnetic fields.

Brain tumors seemed to aggregate in the occupations of shunting yard engineer and train attendant. These two occupational groups may have a common exposure that causes brain tumors. However, it is unlikely that electromagnetic fields are solely responsible for this finding. We did not find a dose-response relation between exposure to ELF magnetic fields and risk of brain tumor mortality. Speculatively, the results shown in table 5 could be interpreted to mean that risk of brain tumor mortality exhibits a threshold with respect to ELF magnetic field exposure. We found elevated brain tumor rates for occupations that in other studies had been found to entail exposure to the highest electric fields: shunting yard engineers and train attendants. Hence, our results fit in with Guénel et al.'s (23) conclusion that brain cancer risk relates more to electric field exposure than to magnetic field exposure. However, Guénel et al.'s findings were not confirmed by Miller et al. (24).

Limitations

In this study, there was potential for exposure bias from several sources. Measurements were done in different ways for the four occupational groups. The effect of this was probably minor, since the largest potential for bias was with the occupations of generally low exposure: These were measured least precisely. Historical extrapolation could be based on erroneous judgment about past exposures, either over- or underestimating exposures. It is hard to assess the possible effect of this, except that the relative order of occupations with respect to exposure would probably be preserved. In view of the above discussion, the nonassessment of electric field exposure must be considered a weakness.

Ascertainment of death

Probabilistic record linkage poses the problem of false positives (false links) and false negatives (missed links). With the restrictive strategy we used, the numbers of deaths and causes linked to the wrong person were certainly small. From the manual verification of cancer deaths, in which we found one person still alive among 122 deaths checked, we estimate it to have been less than 1 percent. On the other hand, we probably missed some deaths, which reduced the power of our study as well as the size of the estimated effects of ELF magnetic fields. The number of deaths missed was probably less than 4 percent, since most of these deaths would have been found among the 147 additional deaths linked when less restrictive linkage rules were applied. We can discern no reason why these losses should have differed according to occupation. Ascertainment of causes of death such as leukemia and (especially) brain cancer may be subject to errors. A validation study showed that the quality of cause-of-death data was good for leukemia and fairly good for brain tumors (see Materials and Methods section).

Exposure assessment

We had employment data, including duration and type of activity, for all members of our cohort. All of the major engines that had ever been in use were measured repeatedly so that exposure could be assessed precisely, and extrapolation was fairly straightforward. Taken together, this means that in the present study, accurate exposure assessment was possible for the highly exposed group. For the less exposed groups of station masters and train attendants, the relative accuracy is lower. Because newer electric and electronic equipment, most notably air conditioning in coaches (since 1964) and computers in station offices (since 1985), was introduced rather recently, the linear historical interpolation used probably led to an overestimate of the historical exposure of these groups, decreasing any estimate of the effects of ELF magnetic fields. However, for these occupations as well, the absolute level of exposure was determined fairly accurately (±1 μT-years).

The data logging at 10-second intervals permitted us to quantify and investigate the health effects of length of time spent under magnetic fields of ≥10 μT, in addition to the more customary cumulative exposure. In a crude way, this measure describes the dynamics of the exposure process. We neglected leisure time and home exposures, because we judged them to be negligible in comparison with occupational exposures.

Confounder assessment

From the information obtained about the substances used for cleaning and maintenance, there seems to be no reason to suspect any confounding effect. A substudy showed that line engineers smoked less than either shunting yard engineers or train attendants. Line engineers, working mostly alone in their driver's stands, tend to have fewer contacts with other people than workers in the other occupations investigated. Both of these characteristics reduce the exposure of line engineers to two suspected (but not well established) causes of leukemia.

Comparison with literature

Comparison of our study with other occupational or residential studies in the literature is complicated somewhat by the fact that most other studies were concerned with the effects of 50- or 60-Hz alternating current on health, while in our study, 16⅔ Hz was the frequency assessed. It is instructive to compare our study with three other studies (7, 25, 26) of railway personnel exposed to 16⅔-Hz ELF magnetic fields. Table 7 provides a comparison with these studies.

The similarities between these studies with respect to both the occupational risk profiles for leukemia and brain tumors and the exposure situation are remarkable. Swiss and Swedish railway engineers show substantially elevated risks of leukemia, which is also observed among Norwegian tram drivers. This supports the notion of the importance of dynamic exposure aspects. Swiss shunting yard engineers and train attendants, Swedish conductors, and Norwegian track walkers have elevated brain tumor risks, which suggests a risk of continuous long term exposure to electric and magnetic fields. However, several major distinctions should be borne in mind: first, the lower exposures of Swedish railway employees compared with Swiss (there were no exposures given for the Norwegian railway workers) and, second, differences in reference groups. Both factors could be expected to lead to a reduction in risk among the Swedish workers relative to the Swiss workers. Third, there are differences in study sizes, as well as in distribution of diagnoses: The Swiss study had more power to detect effects on leukemia in engineers, while the Swedish one had more power for brain tumors. Fourth, the ratio of the number of cases of leukemia to the number of cases of brain tumors ranged from nearly 5 in Swiss line engineers to 0.4 in Swedish conductors.

We are aware of two occupational studies besides this one that permit the estimation of a dose-response relation (4, 10). Table 8 summarizes the findings of these studies. There is no statistical disagreement between the findings of the present study and those of Floderus et al. (4), but there is statistical disagreement with the findings of Tynes et al. (10). However, the latter study reported results on exposure that are difficult to reconcile with each other: A yearly average exposure of 20 μT (10, p. 647) would necessitate 95 years of exposure for accumulation of 1,900 μT-years, which is the border between the highest and second highest exposure categories in Tynes et al.'s table 3 (10, p. 650).

Several factors lead us to believe that the accuracy of our assessment of line and shunting yard engineers' exposure in the present study was quite good. First, line and shunting yard engineers spend a large fraction of their working time in the same, fixed location, which permits accurate assessment of exposure. Thus, daily workplace exposures could be measured exactly as they had occurred over the past 50 years, using the same engines and measuring at the driver's position. Second, reconstruction of group exposures relied on these measurements and on historical records of numbers of engines in use. We know of no other study in which similar features could be exploited to obtain accurate exposure assessment. Assessment of train attendants' and station masters' exposure was less accurate, since only recent exposure situations could be measured for these occupations.

The findings of the present study do not result from data-dredging, because we evaluated two hypotheses formulated a priori (see Introduction).

The frequency of 16⅔ Hz has some special interest in view of findings on a frequency-dependent calcium efflux from cells at the frequency of 15 Hz and multiples thereof (27). Another mechanism of cancer promotion being discussed is based on melatonin, since melatonin appears to be involved in modulation of the immune system (28) and has oncostatic properties (29). In a related study, the melatonin metabolism of locomotive engineers was investigated (19). This study showed a suppression effect after onset of exposure which could not be explained by the shift work. Comparable findings were reported by Burch et al. (30). Thus, a possible pathway of leukemia causation is a disturbance of melatonin metabolism.

Conclusions

This study contributes to the evidence that exposure to ELF magnetic fields in high dosages over prolonged time promotes or generates leukemia. The best estimate of the dose-mortality relation is an increase of approximately 1 percent per μT-year of cumulative thorax exposure. On a methodological level, this study reinforces the impression that accurate assessment of electromagnetic field exposure through historical reconstruction is crucial. With the moderate size of the risks involved and the rarity of leukemia and brain tumors, even moderate exposure misclassification will invariably lead to insignificant results.

What are the consequences of this study and similar studies with respect to prevention? We believe that moni-

TABLE 7. Results of four studies on leukemia, brain tumors, and exposure to 16⅔-Hz electromagnetic fields

Swiss railway cohort, 1972–1993 (current study)				Floderus et al., 1994 (7)				Tynes et al., 1992 (25)			Alfredsson et al., 1996 (26)			
Occupation	Exposure†	No.	RR‡	Occupation	Exposure§	No.	RR¶	Occupation#	No.	SIR‡,**	Occupation	Exposure††	No.	RR¶
Leukemias (ICD-8 codes 204–207)*														
Line engineer	17.9	19	2.4	Railway engine driver	4.0	6	1.6	Railway engine driver	4	1.0	Railway engine driver	15	15	1.2
Shunting yard engineer	13.4	3	2.0					Tram driver	4	1.4				
Train attendant	1.9	9	1.1	Conductor	0.6	7	1.1				Conductor	7	5	1.6
Station master‡‡	0.6	6	1.0	Railway worker	0.3	17	1.2	Railway track walker	13	0.9				
Brain tumors (ICD-8 code 191)														
Line engineer	17.9	4	1.02	Railway engine driver	4.0	8	1.1	Railway engine driver	5	0.44	Railway engine driver	15	10	1.0
Shunting yard engineer	13.4	5	5.06					Tram driver	6	2.04				
Train attendant	1.9	11	2.67	Conductor	0.6	16	1.3				Conductor	7	2	0.8
Station master‡‡	0.6	3	1.00	Railway worker	0.3	31	1.2	Railway track walker	12	2.20				

* ICD-8, *International Classification of Diseases*, Eighth Revision (18).
† Mean exposure (μT) in 1960 (table 3).
‡ RR, risk ratio; SIR, standardized incidence ratio.
§ Daily mean exposure (μT).
¶ Risk ratio relative to all males aged 20–64 years and working in 1960.
# From group II (i.e., long term exposure).
** Standardized for age.
†† Mean exposure (μT).
‡‡ Reference category.

TABLE 8. Results of three studies showing a dose-response relation between exposure to extremely low frequency electromagnetic fields and leukemia risk

Study	% increase in risk per μT-year	95% confidence interval	Comments
Swiss railway cohort, 1972–1993 (current study)—table 6	0.94	0.23,1.65	Based on thorax exposure. Typical exposure, 15 μT.
Floderus et al., 1993 (4)—table 3*	6.2†	–13.1, 30.0	Twenty years' exposure assumed. Typical exposure, 0.2 μT.
Tynes et al., 1994 (10)—table 3	–0.02†	–0.13, 0.08	Based on midpoints of exposure categories. Typical exposure, 20 μT.

* Primarily 50-Hz exposures.
† Computed using weighted regression.

toring of electromagnetic field exposure is indicated for railway personnel, both to maintain their health and to prevent an accentuation of risk through further increases in exposure.

ACKNOWLEDGMENTS

This study was supported by a grant (32-32459.91) from the Swiss National Science Foundation.

The authors thank N. Antille, M. Bräuchi, G. Burkard, T. Furrer, M. Gerber, Dr. R. Gränicher, P. Kurth, E. Mathez, D. Reichen, D. Schneider, and J. P. Terrapon of the Swiss Federal Railways for their help with data access and data acquisition. They acknowledge the various Swiss tumor registries and hospital pathology centers for verifying the diagnoses. The authors also thank Drs. T. Abelin, M. Egger, R. Gugelmann, G. Schüler, and A. Stuck for their many valuable comments and suggestions.

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